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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,941	10/14/2003	Chin-Ming Chang	17501CON1 (AP)	7685

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/685,941	CHANG ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/02/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed 05/02/06, claim 26 has been amended; claims 27-30 have been cancelled; and claim 31 has been newly added. Claims 26 and 31 are currently pending for prosecution on the merits.

Summary of Action

2. The rejection of claims 26-30 under 35 U.S.C. 103(a) as being unpatentable over Yuksel et al. (Ophthalmologica, 1999, 213(4), 228-233) is not maintained in light of the amendment.

3. The provisional rejection of claims 26-30 under the judicially created doctrine of double patenting over claims 54-57 of copending Application No.10/126,790 is maintained for the reasons of record. No Terminal Disclaimer has been filed and approved in our PTO record.

4. Applicant's amendment requiring "said composition is administered twice a day or less often" requires a new ground of rejection(s) in this Office Action.

Response to Arguments

5. Applicant's arguments with respect to claims 26-30 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 26 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claim 26 introduces new limitation into the claimed invention: the claim 26 recites that the claimed composition is administered twice a day or "less often". The interpretation of the instant claim allows for the administration of said composition in less (The American Heritage Dictionary, Second College Edition, 1982 defines the term "less" as "not as great in amount of quantity or consisting of a smaller number") than twice a day, for example once a day, half drop a day, quarter drop a day, once a week or once a month.

The examiner determines that when all evidences in the original disclosure are considered and carefully reviewed, the amended claim fails to find support in the original specification.

The specification discloses that the composition of the present invention is administered in twice a day (page 3, lines 7 and 15-16; Example II). The specification discloses that adequate lowering of intraocular pressure has been obtained when administering the compositions of this invention twice a day as compared to the FDA-approved regimen wherein brimonidine is administered three times a day and timolol is administered twice a day (page 4, lines 7-11). Particularly, in page 16, lines 4-10 of the instant specification, the specification provides tests and discloses that the combination treatment administered twice a day (BID) for 3 months was

superior to timolol BID and brimonidine TID in lowering the elevated IOP of patients with glaucoma or ocular hypertension.

In light of the instant specification, one having ordinary skilled in the art would have understood that the lowering of the elevated IOP of patients with glaucoma or ocular hypertension is only sufficiently achieved by twice a day (BID) administration of said composition, not less than twice a day. There is no express statement or demonstrated tests that the administration of said composition "less often" than twice a day would be able to achieve the desired effects of the claimed invention.

As stated above, the specification only states about the boundaries of the claim as to the twice a day administration. There is no express statement about "less often" that can be found in the specification. Thus, the inclusion of "less often recited in the present claims, which did not appear in the specification filed, introduces new concepts and violate the description requirement of the first paragraph of 35 USC 112.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 26 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 26 recites that the claimed composition is administered "twice a day or less often". The term "less often" in claim 26 is a relative term which renders the claim

indefinite. The term "less often" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

In ophthalmic formulation art, when drug(s) is/are delivered in the form of eye dropper, said drug(s) is/are instilled to the affected eye in drop(s) over certain period of time, for example one drop in the affected eye once a day (QD), twice a day (BID), once a two days and once a week. Since the interpretation of the instant claims allow for the inclusion of the administration of said composition once a day, once or twice over two days, once or twice over three days, once or twice over four days, once a week and etc..., applicant's recitation of "less often" leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 26 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larsson (Arch Ophthalmol., Vol. 119, 2001, pp. 492-495) in view of Bandyopadhyay et al. (US 2002/0128267 A1).

The amended claims read on a method of treating glaucoma or ocular hypertension comprises topically administering a therapeutically effective amount of a single composition comprising about 0.2% by weight of brimonidine and about 0.5% by weight of timolol in a pharmaceutically acceptable carrier thereof, to the affected eye, wherein said composition is administered twice a day or less often. Further limitation includes "brimonidine is administered only in the composition" (claim 31).

Larsson teaches the topical administration of 0.2% brimonidine with 0.5% timolol, alone and in combination, for the treatment of glaucoma by lowering intraocular pressure (see page 493, column 1, line 24 thru column 2, line 5 under the heading of "Subjects and Methods"), wherein brimonidine and timolol is administered twice a day, for example brimonidine is administered separately 5 minutes apart from the administration of timolol.

Bandyopadhyay is being supplied as a reference to demonstrate the state of art knowledge in formulating pharmaceutical combination of active agents (e.g., brimonidine, timolol, COX-2 inhibitor, etc...) in separate composition or a single composition, including topical ophthalmic formulation (see, para. [0411], [0507], [0512], [0513], [0514], [0123] and [0127]). Bandyopadhyay also teaches the advantage of delivering drugs in combination including "the reduction of side effects of the individual therapeutic compounds", "greater patient compliance" and/or "maximize the therapeutic effect at higher dose" when compared to the monotherapy (see para. [0510]-[0511]).

The teaching of Larsson differs from the claimed invention in the administration of brimonidine and timolol in a single composition. To incorporate such teaching into the teaching of Larsson, would have been obvious in view of Bandyopadhyay who teaches the state of art knowledge in preparing pharmaceutical combination of active ingredients (including brimonidine and timolol) which are intended for ophthalmic therapeutic application in separate composition or a single composition.

As discussed above, Larsson makes clear that brimonidine and timolol have been used alone or in combination for the treatment of glaucoma by lowering IOP. Furthermore, Bandyopadhyay makes clear that determination of formulating two compositions each of which is taught by prior art to have common utilities in a single composition or separate composition is well within the skill of artisan. Thus, one having ordinary skill in the art would have been motivated to make such modification to increase the efficacy of drugs and extend the usage of said drugs by making brimonidine and timolol in a single composition to accommodate patient's

preference and needs where the compliance could be improved by delivering the drugs in single application.

One having ordinary skill in the art would have been motivated at the time of the invention was made to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 26 and 31 are provisionally rejected under the judicially created doctrine of double patenting over claims 54-57 of copending Application No.10/126,790, which has been allowed, but not yet patented. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other: both the instantly claimed subject matter and the copending application are drawn to a method for treating glaucoma or ocular hypertension administering a composition comprising

brimonidine and timolol in a pharmaceutically acceptable carrier in same concentration of about 0 0.2% by weight of brimonidine and about 0.5% of timolol in a single composition, wherein the administration frequency of the instant claims differ from the copending application by reciting "twice a day or less often". Since the scope of the copending "twice a day" administration overlaps with the instantly claimed "twice a day or less often", the copending application makes obvious the instant claims.

With respect to the obviousness over the copending claims 55 and 56, since the interpretation of the instant claims allow for the inclusion of any other unspecified ingredients even in major amounts, the copending application containing benzalkonium makes obvious the instant claims.

With respect to the obviousness over the copending claim 57, although the copending application is directed to the method of reducing the number of daily topical ophthalmic doses of brimonidine, the claimed invention in claim 57 is achieved by the administration of same compound in same dosage amount to same treatment group (e.g., glaucoma or ocular hypertension) in overlapping administration frequency. Therefore, the copending application makes obvious the instant claims.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. No Claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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